REMARKS

Reconsideration of this application is requested. Claims 9-24 are pending in the application of which claims 13, 14, 16-18 and 20 are under active examination while claims 9-12, 15, 19 and 21-24 are withdrawn from consideration

Claims 17, 18 and 20 are rejected as being anticipated by U.S. patent 4,404,289 to Masuda et al or U.S. patent 4,405,711 also to Masuda et al.

The Official Action argues that the '289 patent discloses methods for immunochemical measurement of a trace component--this is not the case. This patent relates to materials used as spectral sensitizers for photographic use to label trace components such as an antigen or antibody. Spectral sensitizers are well known for photographic films and when coated on silver halide particles they sensitize the particles to light; however, spectral sensitizers are not luminescent. By contrast, the claims of the present application are directed to luminescently labeled components of an aqueous liquid which includes a luminescent dye which is detectable by luminescence and is of the type defined in the claims, notably claim 17. Claim 17 has been amended to specify that the luminescent dye is detectable by luminescence to emphasize this point.

The same observations apply to the '711 reference which contains a similar discussion at column 10, lines 51-59 as to spectral sensitizers which are comparable to the discussion at column 10, lines 3-9 of the '289 patent.

Accordingly, claims 17, 18 and 20 define subject matter that is novel over the disclosures of either of these two citations.

Claims 17, 18 and 20 are also rejected as being anticipated by the 1981 abstract of Waggoner et al. The senior author of this abstract is the inventor in respect of the present application.

Claims 17-18 and 20 are rejected as being anticipated by Waggoner, A.S. et al, Biophysical Journal, Vol 33, page 292a, (1981). This abstract discloses that the reactive sulfhydryl group on the F1 region of cattle rhodopsin has been covalently labeled with a

cyanine dye. The precise structural features of the cyanine dye used to label this molecule are not specified.

Claim 17 of the present application (as amended) relates to a luminescently labeled component of an aqueous liquid comprising a luminescent dye detectable by luminescence and selected from cyanine merocyanine or styryl dyes containing at least one sulphonate or sulphonic acid group attached to an aromatic nucleus, the dye being covalently reactive with and being bound to the component.

Claim 20 relates to a protein, nucleic acid, cell, sugar or carbohydrate having at least one amino or hydroxyl group labeled with a luminescent cyanine dye.

Applicant submits claims 17, 18 and 20 are novel. As to claim 17, Waggoner et al does not disclose all of the features of claim 17 because the document does not disclose that the dye selected from the group consisting of cyanine merocyanine and styryl dye must contain at least one sulphonate or sulphonic acid group. Clearly a claim to a luminescently-labeled component labeled with a luminescent dye having a requirement for a specific structural feature, namely a sulphonate or sulphonic acid group, is not anticipated by a general disclosure of a cyanine dye in the Waggoner et al abstract. Claim 17 is therefore believed novel over this document.

Waggoner et al does not disclose all of the features of claim 20 because the document does not disclose components (protein, nucleic acid, cell, sugar or carbohydrate) that contain at least one amino or hydroxyl group. By contrast, the only structural requirement of the F1 region of the rhodopsin molecule is the presence of a reactive sulfhydryl group, thus suggesting that the dye is derivatized such that it is only covalently reactive with this group. Claim 20 is therefore novel over Waggoner et al.

In addition, although not raised in the Action, claims 17, 18 and 20 are inventive over Waggoner et al. The differences between the Waggoner et al reference and claim 17 are that:

i) the luminescently labeled component is water soluble (since it is present in an aqueous liquid) and

ii) the dye moiety must contain at least one sulphonic acid or sulphonate group attached to an aromatic nucleus.

Starting from this prior art, the problem to be addressed by the skilled person is the generation of a range of luminescently-labeled target materials that may be present as components in an aqueous liquid, and labeled with a luminescent dye selected from the particular classes of dyes indicated. The solution to the problem is the luminescently-labeled component according to claim 17.

As stated above, Waggoner et al relates to labeling of the F1 region of rhodopsin with a cyanine dye, and to the dye-labeled rhodopsin molecule. Applicant submits that this disclosure is non-enabling, firstly because there are no experimental details in the abstract to indicate the conditions used for labeling, and secondly, because the abstract is silent on the precise structure of the cyanine dye. The skilled person therefore has no technical information nor guidance to provide a starting point for modifying the labeled rhodopsin as disclosed in Waggoner et al, in order to arrive at the dye-labeled component as claimed in claim 17.

It is clear from the wording of claim 17, that the labeling dye must be capable of labeling a target material in an aqueous medium, and be sufficiently versatile so as to be capable of labeling targets having different functional groups (and not just those containing a reactive sulfhydryl group).

As stated above, the Waggoner et al disclosure is in the form of an abstract only and no information is given to the skilled person regarding the conditions under which the labeling at the reactive sulfhydryl is performed. The Waggoner et al disclosure reports, (in the context of an enzyme cascade mechanism for visual excitation), that conformational changes of the dye-labeled rhodopsin affects the absorbance of the dye. However, the disclosure does nothing to address the wider issue of the use of bright fluorescent dyes for applications in labeling and detection of a range of target materials. The Waggoner et al disclosure offers the skilled person no technical guidance and no motivation to modify its teachings to address this issue.

By contrast, the present invention results from the surprising discovery that, by attaching at least one sulphonate or sulphonic acid group to the aromatic nucleus of a cyanine or related dye, the tendency of such dyes to form aggregates is minimized. This has the beneficial result that the emitted fluorescence is brighter with such dyes, than with non-sulphonated dyes of the same class.

Applicant submits that the Waggoner et al disclosure does not lead the skilled person to the invention as claimed in claim 17 and that this claim (and its dependent claim 18) is non-obvious and inventive.

The difference between the Waggoner et al reference and claim 20 is that the target material requires at least one amino or hydroxyl group suitable for labeling.

Again, starting from this prior art, the problem to be addressed by the skilled person is the generation of a target molecule (protein, nucleic acid, etc) labeled with a luminescent cyanine dye.

Waggoner et al teaches only that a sulphydryl group of the F1 region of rhodopsin has been labeled with a cyanine dye and that a conformational change of the rhodopsin molecule affects the absorbance of the dye. The disclosure does nothing to address the issue of fluorescent cyanine dyes for use in applications in labeling and detection of a range of target materials. The Waggoner et al disclosure provides no technical guidance, nor motivation to modify its teachings to address this issue and the skilled person would not have started from this disclosure.

Hence, the Applicant contends that invention as claimed in claim 20 is non-obvious and inventive over Waggoner et al.

All of the now pending claims are rejected on the basis of obviousness-type double patenting over claims of various U.S. patents in the series; see items 15-18 of the Official Action. Counsel wishes to have these double patenting rejections held in abeyance until other issues are resolved and the claims are found to be allowable but for such objections.

Reconsideration and favorable action are solicited.

Attached hereto is a marked-up version of the changes made to the claim by the current amendment. The attached page is captioned "**Version With Markings To Show Changes Made.**"

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS

17. (Amended) A luminescently labeled component of an aqueous liquid comprising a luminescent dye detectable by luminescence and selected from the group consisting of cyanine, merocyanine and styryl dyes containing at least one sulphonate or sulphonic acid attached to an aromatic nucleus said dye being covalently reactive with and being bound to said component.